

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 864

DMB

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Certifier D. Hawkins

[Docket No. 96P-0484]

Medical Devices; Hematology and Pathology Devices; Reclassification of Automated Blood Cell Separator Device Operating by Filtration Principle from Class III to Class II

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is reclassifying the automated blood cell separator (ABCS) device operating by filtration principle, intended for routine collection of blood and blood components, from class III to class II (special controls). The special control requirement for this device is an annual report with emphasis on adverse reactions to be filed by the manufacturer for a minimum of 3 years. The agency is taking this action in response to a petition submitted under the Federal Food, Drug, and Cosmetic Act (the act) as amended by the Medical Device Amendments of 1976 (the 1976 amendments), the Safe Medical Devices Act of 1990 (the SMDA), and the Food and Drug Administration Modernization Act of 1997 (FDAMA). The agency is reclassifying the automated blood cell separator devices operating by filtration principle into class II (special controls) because special controls, in addition to general controls, are capable of providing a reasonable assurance of safety and effectiveness of the device.

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96P-0484

NFR-1

DATES: This rule is effective [*insert date 30 days after date of publication in the Federal Register*].

FOR FURTHER INFORMATION CONTACT: Paula S. McKeever, Center for Biologics Evaluation and Research (HFM-17), Food and Drug Administration, 1401 Rockville Pike, Rockville, MD 20852-1448, 301-827-6210.

SUPPLEMENTARY INFORMATION:

I. Background

The act (21 U.S.C. 301 *et seq.*), as amended by the 1976 amendments (Public Law 94-295), the SMDA (Public Law 101-629), and FDAMA (Public Law 105-115), established a comprehensive system for the regulation of medical devices intended for human use. Section 513 of the act (21 U.S.C. 360c) established three categories (classes) of devices, depending on the regulatory controls needed to provide reasonable assurance of their safety and effectiveness. The three categories of devices are class I (general controls), class II (special controls), and class III (premarket approval).

Under section 513(f)(1) of the act, devices that were not in commercial distribution before May 28, 1976, the date of enactment of the 1976 amendments, generally referred to as postamendments devices, are classified automatically by statute into class III without any FDA rulemaking process. Those devices remain in class III and require premarket approval, unless and until the device is reclassified into class I or II or FDA issues an order finding the device to be substantially equivalent, under section 513(i) of the act, to a predicate device that does not require premarket approval. The agency determines whether new devices are substantially equivalent to previously

offered devices by means of premarket notification procedures in section 510(k) of the act (21 U.S.C. 360(k)) and 21 CFR part 807.

Under section 513(f)(3) of the act, FDA may initiate the reclassification of a device classified into class III under section 513(f)(1), or the manufacturer or importer of a device may petition the Secretary of Health and Human Services for the issuance of an order classifying the device in class I or class II. FDA's regulations in § 860.134 (21 CFR 860.134) set forth the procedures for the filing and review of a petition for reclassification of such class III devices. In order to change the classification of the device, it is necessary that the proposed new class have sufficient regulatory controls to provide reasonable assurance of the safety and effectiveness of the device for its intended use.

II. Regulatory History of the Device

The AUTOPHERESIS-C SYSTEM, an ABCS, intended for the routine collection of blood and blood components, is a postamendments device classified into class III under section 513(f)(1) of the act. Therefore, the device cannot be placed in commercial distribution for the routine collection of blood and blood components unless it is reclassified under section 513(f)(3) of the act, or subject to an approved premarket approval application (PMA) under section 515 of the act (21 USC 360e). FDA is taking this action under section 513(f)(3) of the act and § 860.134, based on information submitted in a petition by Baxter Healthcare Corp. (Baxter) on June 17, 1996, requesting reclassification of the AUTOPHERESIS-C SYSTEM, intended for routine collection of blood and blood components, from class III to class II (Ref. 1). Although Baxter submitted its petition for reclassification under section 513(e) of the act, the request should have been submitted under section 513(f)(3), and

therefore FDA has considered the petition filed under section 513(f)(3). Consistent with section 513(f)(3) of the act and § 860.134, FDA referred the petition to the Blood Products Advisory Committee, Medical Devices Panel (the Panel) for its recommendation on the requested change in classification. The Panel met on September 26, 1996, at a public meeting (Ref. 2).

III. Device Description

The AUTOPHERESIS-C SYSTEM, intended for routine collection of blood and blood components, is an automated plasmapheresis system. It utilizes a spinning membrane separation device to achieve rapid and gentle separation by filtration of whole blood into concentrated cellular components for reinfusion and into plasma for collection.

The instrument uses a system of pumps and sensors controlled by a microprocessor and it incorporates a variety of safety and alarm system functions. It uses a fully automated processing program to collect a preset volume of plasma from a donor. Plasma collection in the AUTOPHERESIS-C SYSTEM involves sequential phases of collection of plasma from the donor and reinfusion of the residual red blood cell concentrate back to the donor.

The AUTOPHERESIS-C SYSTEM is currently employed in plasma centers where it is used to collect Source Plasma, and it is also found in blood centers and hospital blood banks where it is used for the collection of plasma for preparation of fresh frozen plasma.

Any change in the indication for use, i.e., for therapeutic use, would require a PMA because devices for therapeutic use are not included in this reclassification action.

IV. Risks to Health

FDA has identified the following risks associated with apheresis blood donation and processing: (1) The potential loss of blood due to leaks; (2) thrombosis due to activation of factors by foreign surfaces; (3) toxic reaction to citrate or heparin anticoagulant; (4) damage to red cells, activation of complement, and denaturation of proteins; (5) potential for sepsis and fever due to bacterial contamination of the donor's blood returned to the donor; (6) infectious disease risk to the donor or to the operator due to leaks; (7) electrical shock hazard; (8) donor stress reaction due to removal or loss of blood; and (9) reservoir rupture.

Some of the reported adverse donor reactions are: (1) Allergic reaction; (2) vasovagal or synocopal reaction; (3) citrate toxicity; (4) hematoma; (5) hematuria or hemoglobinuria; (6) hypovolemic reaction; (6) myocardial infarct in three cases unrelated to the donation procedure; (7) mesenteric thrombosis unrelated to the donation procedure; (8) chest pains; (9) high blood pressure; (10) blood clotting; (11) nonresponsive donor during or after the donation procedure; (12) death of a donor several days following an apheresis unrelated to the procedure; (13) blood spray; and (14) tubing separation.

In addition to the potential risks of the AUTOPHERESIS-C SYSTEM and subsequent generic types of filtration-based blood cell separators, there is sufficient information about the benefits of the device. Specifically, the AUTOPHERESIS-C SYSTEM has been used since 1986, and the data presented by Baxter show no evidence of cellular or protein damage to the donor blood; the procedure is well tolerated by the donor; and the instrument is safe and effective for plasma collection. The period from 1986 to 1996 showed that a

0.03 percent of donations were associated with some type of potential adverse event that were reported to Baxter.

V. Panel Recommendation

The Panel reviewed the data and information contained in the petition and provided by FDA, and considered the open discussions during the Panel meeting. The Panel consisted of members with personal knowledge of and clinical experience with the device. At a public meeting on September 27, 1996, the Panel unanimously recommended that the AUTOPHERESIS-C SYSTEM and subsequent membrane-based blood cell separators substantially equivalent to this device, intended for routine collection of blood and blood components, be reclassified from class III to class II. The Panel believed that class II with the special controls of a periodic report filed annually for a minimum of 3 years with emphasis on adverse reactions would provide reasonable assurance of the safety and effectiveness of the device.

VI. Special Controls

FDA believes that, in addition to general controls, the special controls described below address these risks and provide reasonable assurance of the safety and effectiveness of the device. FDA described the special controls in the **Federal Register** of May 29, 2001 (66 FR 29149 at 29151), and provided an opportunity for public comment. FDA did not receive any comments on the special controls. Therefore, on September 5, 2001, FDA issued an order to the petitioner reclassifying the AUTOPHERESIS-C SYSTEM, and substantially equivalent devices of this generic type, from class III to class II subject to the special controls described below (Ref. 3). Through this final rule, FDA is codifying the reclassification of this device by revising 21 CFR

864.9245. By listing the contents of the special controls, new manufacturers of substantially equivalent devices can comply with the same special controls.

In addition to general controls of the act, automated blood cell separator devices operating by filtration principle are subject to the following special controls in order to provide reasonable assurance of the safety and effectiveness of the device. The manufacturer must file an annual report with FDA on the anniversary date of reclassification for 3 consecutive years. A manufacturer of a device determined to be substantially equivalent to the AUTOPHERESIS-C SYSTEM, intended for routine collection of blood and blood components, also is required to comply with the same general and special controls. Any subsequent change to the device requiring the submission of a premarket notification in accordance with section 510(k) of the act should be included in the annual report.

Each annual report (special control) must include:

1. A summary of adverse donor reactions reported by the users to the manufacturer that do not meet the threshold for medical device reporting under 21 CFR part 803;

2. Any change to the device, including but not limited to:

- new indications for use of the device;
- labeling changes, including operation manual changes;
- computer software changes, hardware changes, and disposable item changes, e.g., collection bags, tubing, filters;

3. Equipment failures, including software, hardware, and disposable item failures, e.g., collection bags, tubing, filters.

VII. Environmental Impact

The agency has determined under 21 CFR 25.34(b) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

VIII. Analysis of Impacts

FDA has examined the impacts of the final rule under Executive Order 12866, the Regulatory Flexibility Act (5 U.S.C. 601–612), and the Unfunded Mandates Reform Act of 1995 (2 U.S.C. 1501 *et seq.*). Executive Order 12866 directs agencies to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; distributive impacts; and equity). The agency believes that this final rule is consistent with the regulatory philosophy and principles identified in the Executive order. In addition, the final rule is not a significant regulatory action as defined by the Executive order and so is not subject to review under the Executive order.

Under the Regulatory Flexibility Act, if a rule has a significant economic impact on a substantial number of small entities, an agency must consider alternatives that would minimize the economic impact of the rule on small entities. Reclassification of the affected devices from class III to class II will relieve manufacturers of the cost of complying with the premarket approval requirements of section 515 of the act, and may permit small potential competitors to enter the marketplace by lowering their costs. Although the final rule requires manufacturers of these devices to file an annual report with FDA

for 3 consecutive years, this is less burdensome than the current premarket approval requirement that annual reports be submitted to FDA on an ongoing basis. The agency, therefore, certifies that the final rule will not have a significant economic impact on a substantial number of small entities. Therefore, under the Regulatory Flexibility Act, no further analysis is required. In addition, the Unfunded Mandates Reform Act does not require FDA to prepare a statement of costs and benefits for the final rule because the rule will not impose costs of \$100 million or more on State, local, and tribal governments in the aggregate, or the private sector, in any one year (adjusted annually for inflation).

IX. Paperwork Reduction Act of 1995

This final rule contains no collections of information. Therefore, clearance by the Office of Management and Budget under the Paperwork Reduction Act of 1995 is not required.

X. Federalism

FDA has analyzed this final rule in accordance with the principles set forth in Executive Order 13132. FDA has determined that the rule does not contain policies that have substantial direct effects on the States, on the relationship between the National Government and the States, or on the distribution of power and responsibilities among the various levels of government. Accordingly, the agency has concluded that the rule does not contain policies that have federalism implications as defined in the Executive order, and, consequently, a federalism summary impact statement is not required.

XI. References

The following references have been placed on display in the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852, and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday.

1. Petition for reclassification of the Autopheresis-C System from class III to class II by Baxter Healthcare Corp., June 17, 1996.
2. Transcript of the Blood Products Advisory Committee, 52d Meeting, September 27, 1996.
3. Order to the petitioner, September 5, 2001.

List of Subjects in 21 CFR Part 864

Blood, Medical devices, Packaging and containers.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, 21 CFR part 864 is amended as follows:

PART 864—HEMATOLOGY AND PATHOLOGY DEVICES

1. The authority citation for 21 CFR part 864 continues to read as follows:

Authority: 21 U.S.C. 351, 360, 360c, 360e, 360j, 371.

2. Section 864.9245 is amended by redesignating paragraphs (b) and (c) as paragraphs (c) and (d), respectively, by adding new paragraph (b), and by revising newly redesignated paragraphs (c) and (d) to read as follows:

§ 864.9245 Automated blood cell separator.

* * * * *

(b) *Classification of device operating by filtration separation principle.*

Class II (special controls). The special controls for the device are that the manufacturer must file an annual report with FDA for 3 consecutive years.

Each annual report must include the following:

(1) A summary of adverse donor reactions reported by the users to the manufacturer that do not meet the threshold for medical device reporting under part 803 of this chapter;

(2) Any change to the device, including but not limited to:

(i) New indications for use of the device;

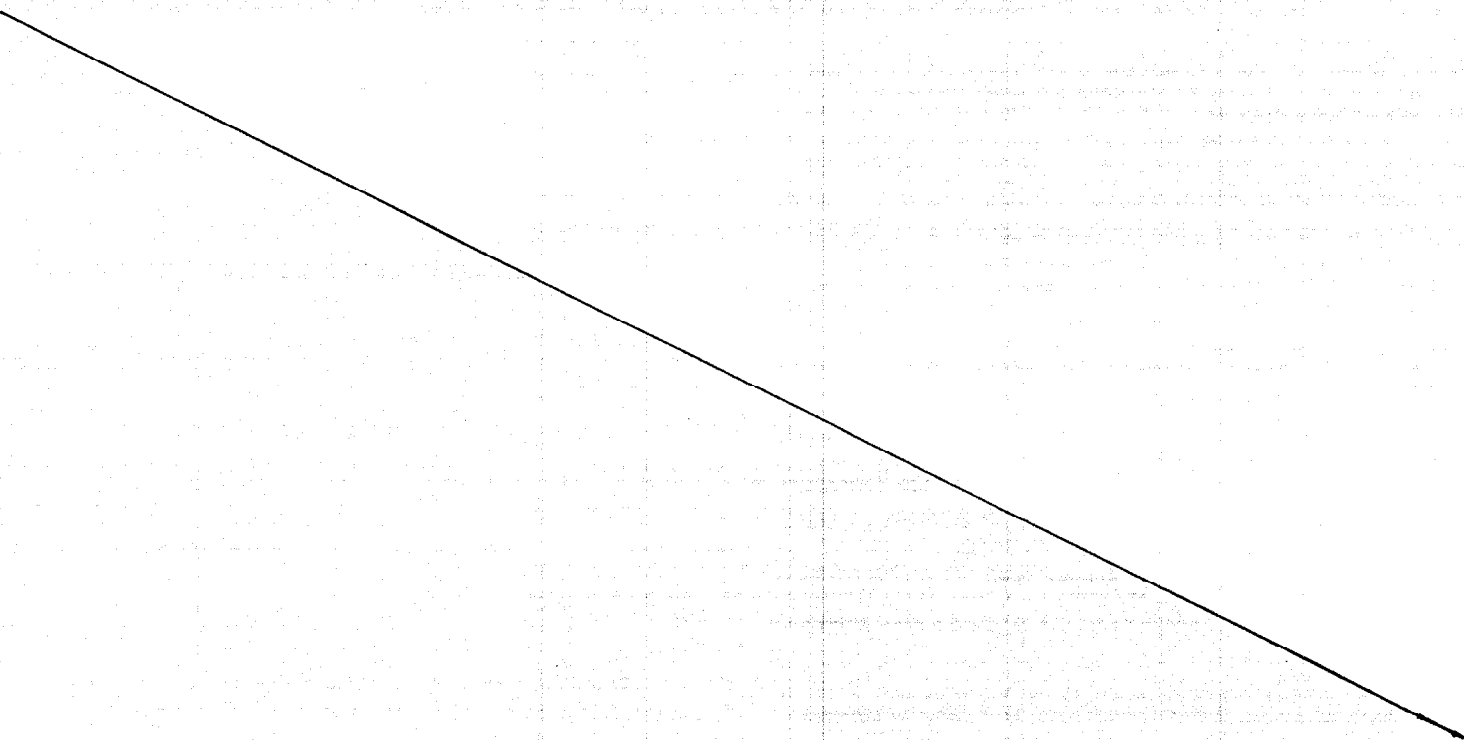
(ii) Labeling changes, including operation manual changes;

(iii) Computer software changes, hardware changes, and disposable item changes, e.g., collection bags, tubing, filters;

(3) Equipment failures, including software, hardware, and disposable item failures, e.g., collection bags, tubing, filters.

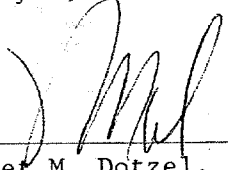
(c) *Classification of device operating by centrifugal separation principle.*

Class III (premarket approval).



(d) *Date PMA or notice of completion of a PDP is required.* No effective date has been established of the requirement for premarket approval for the device described in paragraph (c) of this section. See § 864.3.

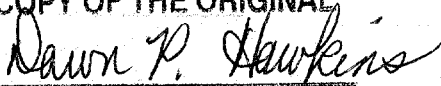
Dated: 2/4/03
February 4, 2003.


Margaret M. Dotzel,
Assistant Commissioner for Policy.

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Dawn P. Hawkins